Bisphosphonate as a Countermeasure to Space Flight-Induced Bone Loss

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The purpose of this research is to determine whether anti-resorptive pharmaceuticals such as bisphosphonates, in conjunction with the routine in-flight exercise program, will protect ISS crewmembers from the regional decreases in bone mineral density and bone strength and the increased renal stone risk documented on previous long-duration space flights [1-3]. Losses averaged ~ 1 to 2 percent per month in such regions as the lumbar spine and hip. Although losses showed significant heterogeneity among individuals and between bones within a given subject, space flight-induced bone loss was a consistent finding. More than 90 percent of astronauts and cosmonauts on long-duration flights (average 171 days) aboard Mir and the ISS, had a minimum 5 percent loss in at least one skeletal site, 40 percent of them had a 10 percent or greater loss in at least one skeletal site, and 22 percent of the Mir cosmonauts experienced a 15 to 20 percent loss in at least one site. These losses occurred even though the crewmembers performed time-consuming in-flight exercise regimens. Moreover, a recent study of 16 ISS astronauts using quantitative computed tomography (QCT) demonstrated trabecular bone losses from the hip averaging 2.3 percent per month [4]. These losses were accompanied by significant losses in hip bone strength that may not be recovered quickly [5].

This rapid loss of bone mass results from a combination of increased and uncoupled remodeling, as demonstrated by increased resorption with little or no change in bone formation markers [6-7]. This elevated remodeling rate likely affects the cortical and trabecular architecture and may lead to irreversible changes. In addition to bone loss, the resulting hypercalciuria increases renal stone risk. Therefore, it is logical to attempt to attenuate this increased remodeling with anti-resorption drugs such as bisphosphonates. Success with alendronate was demonstrated in a bed rest study [8]. This work has been extended to space flight and two dosing regimens: 1) an oral dose of 70 mg of alendronate taken weekly during flight or 2) a single intravenous (IV) dose of 4 mg of zoledronic acid given several weeks before flight. Currently the study is focusing on the oral option because of NASA's safety concerns with the IV-administered drug. The protocol requests 10 male or female crewmembers on ISS flights of 90 days or longer. Controls are 16 previous ISS crewmembers with QCT scans of the hip performed by these same investigators. The primary outcome measure for this study is hip trabecular bone mineral density measured by QCT, but other measures of bone mass are performed including peripheral QCT (pQCT) and dual-energy x-ray absorptiometry. Serum and urinary bone markers and renal stone risk measured before, during, and after flight are included. Postflight data are currently being collected from 2 ISS crewmembers. Two additional crewmembers will return this spring after ~6-month missions. To date no untoward effects have been encountered.

If it is successful, treatment with bisphosphonate or other anti-resorptive agents could be used to supplement other countermeasures such as exercise. Drug therapy would be particularly important when exercise cannot be used effectively, as after injury or equipment malfunction, or when other crew or equipment constraints limit exercise. Use of a pharmaceutical countermeasure as well as exercise could reduce the amount of time that must be spent on exercise (that is, could increase efficiency) without requiring significant additional hardware, storage space, or cost.

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